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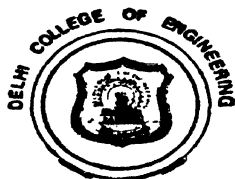
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WE NEED VITAMINS

What Are They?
What Do They Do?

BY

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This presentation answers simply and clearly the following questions concerning each vitamin:

1. What is the vitamin?
2. What are its chemical and physical properties?
3. How is its potency determined and expressed?
4. What does the vitamin do?
5. How does it accomplish this effect?
6. How much of it do we need daily?
7. Where and how can we get it?

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I. What Are Vitamins?

What Food Substances Must We Have?

Our daily food is made up of five kinds of substances:

(1) **Proteins** (meats and meat substitutes) which enable us to build new tissues, such as muscle, bone, nerve, etc.

(2) **Carbohydrates** (starches and sugars) used mainly to supply energy (calories) for the work of the body.

(3) **Fats**, also used as body fuel (calories).

All of these can serve as body fuel, but carbohydrates and fats are *cheaper* than proteins.

(4) **Minerals**, such as iron, calcium (lime), phosphorus, etc., used both to build material for body structures and to control the behavior of body fluids and tissues.

(5) **Vitamins**, or food hormones, required in tiny amounts to *control the body's use* of the above substances and also to protect it from certain specific diseases.

What Are Vitamins?

Vitamins, like proteins, fats, and carbohydrates, are organic, or carbon-containing, chem-

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ical compounds—substances just as definite as sugar or salt. A number of them, of which the following is a list, have been isolated in pure form, chemically identified, and their structure proved by the fact that they can be produced artificially, or as chemists say, “synthetically.” *There is no difference in the physiological action of a pure vitamin whether it is extracted from natural food sources or made synthetically.*

Vitamins Which Have Been Chemically Identified

- Vitamin A (Carotene)
- Vitamin B₁ (Thiamine)
- Vitamin B₂ or G (Riboflavin)
- Vitamin B₆ (Pyridoxine)
- Vitamin C (Ascorbic Acid)
- Vitamin D (Calciferol and 7-dehydro-cholesterol)
- Vitamin E (Alphatocopherol)
- Vitamin H (Biotin)
- Vitamin K (Naphthoquinone Compounds)
- Vitamin P (Erioductiol)
- Nicotinic Acid or Nicotinic Acid Amide
- Pantothenic Acid

At least fourteen others are known to exist but these have not yet been chemically identified.

How Did Vitamins Get Their Names?

In 1911 a Polish chemist, Casimir Funk, isolated from rice polish (a very thin, skinlike coating which covers rice grains, and which is

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removed in preparing the rice of commerce) a crystalline substance which cured the disease known as beri-beri, or polyneuritis. Because these crystals contained the chemical element *nitrogen* combined with *hydrogen*, Funk knew that they were "amines," the chemist's name for compounds containing this combination. Because these particular crystals preserved *life* he called them "vita-amine" or, for short, *vitamine*. When similar substances were discovered, which were also able to cure particular diseases, Funk suggested the general name "Vitamines" for all of them.

In 1913 E. V. McCollum and his assistants extracted from butter and egg fat a substance which, like Funk's crystals, proved to be *necessary to growth*, and also prevented and cured an eye disease known as "dry eye." McCollum declined to call this a "vitamine" because chemical analysis showed that there was no nitrogen in it. For this reason, and because it would dissolve in fats, he gave it the awkward name of "Unidentified dietary factor fat-soluble A." This was the first use of a *letter* to denote these substances. With the discovery of other substances of this class we acquired the terms "water-soluble B and C," "fat-soluble D and E," etc.

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The two methods of nomenclature were combined when J. C. Drummond in 1921 suggested dropping this cumbersome wording, but retaining the letters and preceding them with the term "vitamin"—Funk's term with the "e" removed. Thus the substances became known simply as vitamins A, B, C, D, E, etc.

The next step in naming the vitamins came with discovery of their behavior toward particular diseases; for instance:

Vitamin A became the *anti-"dry eye"* vitamin;

Vitamin B became the *anti-beriberi* or *antineuritic* vitamin;

Vitamin C became the *anti-scurvy* vitamin;

Vitamin D became the *anti-rickets* vitamin.

Present names, however, while not discarding previous terms, tend to be descriptive of the chemical nature of the pure vitamin. Thus vitamin B or B₁ is now known as "thiamine" to indicate its combination of a compound containing nitrogen ("amine") with sulfur ("thio"). Vitamin C is "ascorbic acid." Vitamin G became "riboflavin." For other examples see the vitamin lists.

WHAT ARE VITAMINS?

From the above it is evident that the word "vitamin" describes a group of substances having a common type of physiological *behavior* but differing in their chemical *structure*.

Are Vitamins Foods or Drugs?

No hard and fast distinction can be made. When a physician prescribes vitamin C to cure a case of scurvy he is *using* it as a drug. When he drinks his morning glass of orange juice he is taking the vitamin C in which it is rich as a part of his daily nourishment or *food*. The druggist sells vitamin pills and capsules, but the grocer also sells vitamins in foodstuffs such as fruits, vegetables, cereals, etc.

It seems unimportant therefore to attempt to put these substances into set classifications as foods or as drugs, especially as they can and are taken daily by everyone to protect health without prescription and without need of supervision.

Are They Perishable?

Some of the vitamins are destroyed by taking up *oxygen* from the air; some are destroyed by *heat*, as in cooking; some are destroyed by *light*. Some are not affected by any of the conditions to which foodstuffs are exposed. A few of them

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are affected by the presence of minerals such as copper and iron. Each vitamin, therefore, must be handled in accordance with its peculiarities.

In natural foods the vitamin content of the fresh, raw food may be *reduced* by methods of storage, marketing and cooking. For that reason tables giving the vitamin content of fresh, raw foodstuffs may show values considerably *higher* than those in the foods *when we eat them*.

Because of the peculiarities of each vitamin in respect to perishability, purveyors of these substances in pure form, in fish oils and concentrates, and in foods have been compelled to adopt special measures of protection against deterioration or loss of potency. These precautions may be better discussed under each vitamin reviewed in the succeeding discussions.

Thanks to adequate governmental supervision, the vitamin preparations available to the public in labelled capsules, tablets or enriched foods can be generally relied upon today to deliver the unitage stated on the labels. Retailers of vitamin products should, however, familiarize themselves with the conditions necessary to conserve vitamin potencies and control their products in accordance with this information.

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How Is Vitamin Potency or Content Expressed?

For most of the vitamins sold by drug stores in capsule form, and by grocers and butchers as food, it is now possible to give quantities in units of weight. You can buy vitamin C, for example, by the milligram, gram, or ounce. You can express the vitamin C content of orange juice or tomato juice in milligrams, grams or fractions of an ounce, and similarly for vitamins A, B, C, D, E, etc. But most labels continue to express vitamin content or potency in "units": International Units, U. S. Pharmacopeia Units, Sherman-Bourquin Units, etc. What are these "units"?

Before pure vitamins became available it was necessary to estimate amounts present by the growth or other physiological response of *test animals*. For example, Dr. H. C. Sherman first defined a unit of vitamins A and B as the amount of a source of such vitamins in a diet absolutely free from any other such source, but adequate in all other known nutrient factors, which would produce a gain of 3 grams per week for a period of four weeks in rats previously deprived of all stored vitamin of the type under test. In brief, he worked out a biological test based on *growth effect* to estimate vitamin potency. This is what

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we now call a "bioassay" method. Thus arose expression of potency of vitamins A and B in "Sherman" or "Sherman-Chase" or "Sherman-Munsell" units.

But other scientists devised similar biological tests, and at one time vitamin D potency was expressed in at least four different units: Steenbock units, Poulssen units, American Drug Manufacturers Association units, and rat units. This became very confusing, especially when Viosterol, or vitamin D in oil, became expressed as Viosterol 150 D or 250 D, etc. to indicate that it was 150 or 250 times as rich in that vitamin as cod liver oil. To the layman these terms meant nothing, or merely that one product was so many times as potent as another.

There was need then to eliminate multiplicity of names for units and to make possible the conversion of *units* into *weight of pure vitamin*. This was accomplished by the invention of what are today called *International Units*—units defined by a Committee of the League of Nations and internationally adopted. It was also accomplished by the use of reference materials in bioassays, these materials containing known weights of vitamin. In this country the only other unit terminology is U.S.P. units (United

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States Pharmacopeia units); but so far U.S.P. and International Units are identical.

The following table explains the definitions of units used in labelling drug or food content of vitamins in the United States today:

Vitamin Potency

<i>Vitamin</i>	<i>Unit Definition</i>	<i>Available as Reference Material</i>
A	The amount of source capable of producing the physiological effect of .0006 mg. pure beta-carotene equals one International unit.	U.S.P. Reference Cod Liver Oil containing 1700 International units per gram.
B ₁	The amount of source capable of producing the physiological effect of .003 mg. pure thiamine equals one International unit.	Crystalline thiamine or thiamine chloride.
B ₂ (G)	The amount of source capable of producing the physiological effect of .0025 mg. pure riboflavin is one Sherman-Bourquin unit.	Pure riboflavin.
B ₆	The amount of source capable of curing acrodynia in 3 weeks is the Schneider, Ascham, Platz, Steenbock	Pure pyridoxine.

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(1939) unit. It represents approximately 0.1 mg. B₆ crystals.

C	The amount of source capable of producing the physiological effect of .05 mg. pure ascorbic acid equals one International unit.	Pure ascorbic acid.
D	The amount of source capable of producing the antiricketic effect of .000025 mg. pure calciferol equals one International unit.	Pure calciferol and U.S.P. Reference oil containing 115 International units of D per gram.
E	The amount of source capable in 21 days of rat gestation to insure birth of a litter is an Evans (1922) unit.	Standardized wheat-germ oil.
K	The amount of source required per gram of animal weight on three successive days to bring chick blood clotting time to normal is a Dam (1935) unit.	Standardized alfalfa meal extract and synthetic K ₁ .

For those interested in comparing the preceding unit definitions with those that have been used in the past, the following table also may be of value:

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Vitamin Unit Expressions

(I. U. equals International Unit)

Vitamin A

- 1 I. U. is equivalent to .0006 mg. beta-carotene =
1 U.S.P. unit.
- 1 I. U. is equivalent to 0.7 Sherman unit.
- 1 gram U.S.P. Cod Liver Oil must contain at least
600 I. U. of A per gram.

Vitamin B₁

- | | | |
|---------|---|-----------------------------------|
| 1 I. U. | { | .003 mg. pure thiamine. |
| is | | 2 Sherman-Chase units. |
| equi- | | 0.5 Smith curative unit. |
| valent | | 1.0 Chick-Roscoe unit. |
| to | | 2.0 Cowgill mg. equivalent units. |

Vitamin C

- 1 I. U. is equivalent to .05 mg. ascorbic acid.
- 1 I. U. is equivalent to 0.1 Sherman-La Mer unit.
- 1 cc. ave. orange juice contains approximately 8.5
I. U.

Vitamin D

- 1 I. U. is equivalent to .000025 mg. calciferol = 1
U.S.P. unit.
- 1 I. U. is equivalent to 3.25 A.D.M.A. units.
- 1 I. U. is equivalent to 0.37 Steenbock units.
- U.S.P. Cod Liver Oil must contain at least 85 I. U.
per gram.
- Viosterol must contain at least 10,000 I. U. of vitamin
D per gram.
- Product labelled 250 D or 150 D etc. indicates 250 or
150 times the D content of a potent cod liver oil
used as standard. According to Council of Phar-
macy a Viosterol labelled 250 D contains 3333

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A.D.M.A. rat units per gram or approximately 10,000 I. U. per gram.

Vitamin B₂ or G

1 Sherman-Bourquin unit is equivalent to 2.5 micrograms Riboflavin. (A microgram or gamma is 1/1000th of a milligram.)

How Is Vitamin Potency Measured Today?

Owing to the extremely tiny amounts present in most sources, isolation and actual weighing are impossible. At present there are four laboratory methods in practice:

- (1) Color-measuring tests, in which the color produced by the vitamin reacting with some chemical is compared with solutions of known vitamin content.
- (2) Tests based on ability of vitamins to absorb light of certain wave lengths.
- (3) Tests in which the amount necessary to produce growth or other response in microorganisms such as bacteria, molds, and yeast is compared with the effect of pure vitamin solutions.
- (4) Bioassays. Tests in which *growth response* or cure effects of a given amount of source in test animals such as rats, guinea pigs, and chicks is compared with the effect of known amounts of pure vitamin or reference standards of known vitamin content.

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The only tests so far accepted by the U. S. Food and Drug Division for Vitamins A, B₁, and D are bioassay methods outlined in detail in the U. S. Pharmacopeia and in the Methods of Analysis of the Association of Official Agricultural Chemists (A.O.A.C.). The other methods are in use for control purposes in producing laboratories today and may in time become accepted as official.

What Do Vitamins Do?

This question will be answered in greater detail in the discussions of the properties of the individual vitamins which follow. In general, however, we may express the functions of vitamins as follows:

- (1) To supply building or reconstruction material to certain substances or tissues which the body uses, for example, Vitamin A is used to build or reconstruct the eye pigments used to produce vision.
- (2) To form active groups in certain enzymes and coenzymes which the body uses in its metabolism, or utilization and conversion of foodstuffs.
- (3) To prevent in some manner (not always clearly determined as yet) pathological or

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abnormal changes in body tissues and behavior, for example, Vitamin D in prevention of rickets, Vitamin E in prevention of muscular weakness, Vitamin K in preserving power of blood to clot, etc.

II. Vitamin A

How many forms of this vitamin exist?

Vitamin A₁, found in the liver oils of salt-water fish (cod, halibut, tuna, shark) and in some animal products, such as butter fat, egg yolk, and liver.

Vitamin A₂, found in the livers of fresh-water fish.

Provitamins A, yellow pigments manufactured by plants, especially carotene, the coloring matter of carrots.

What is the difference between Provitamins A and Vitamins A₁ and A₂?

The provitamins are *not active* in the body until *changed* by some enzyme into A₁ or A₂, the active forms. The *active* vitamins A₁ and A₂ are nearly colorless, oily substances, which dissolve in fats and oils, but not in water.

The provitamins are *yellow pigments*, varying in the amounts of active vitamins they can produce. The four known pigments are alpha, beta, and gamma-carotene and cryptoxanthin. (Chemists often use Greek letters to distinguish between different forms of the same substance.) In liver

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oils vitamins A_1 and A_2 occur as alcohols known as *sterols*.

The provitamins occur as *hydrocarbons*, that is, as combinations of the elements carbon and hydrogen.

Does it matter which form of vitamin A we eat?

Yes. Apparently the body can more effectively utilize the active forms (A_1 and A_2) than the inactive provitamins, which have to be *changed* in the digestive tract or liver before the body can use them. Booher, basing her conclusions on human tests, reports that beta-carotene is only 50 to 60% as effective as vitamin A in human nutrition.

What are the properties of the vitamins and provitamins A?

- (1) They differ in the amounts of carbon, hydrogen and oxygen present. For example,
- Vitamin A_1 has 20 carbon, 30 hydrogen and one oxygen atom;
 - Vitamin A_2 has 22 carbon, 32 hydrogen and one oxygen atom;
 - Provitamin A (carotene) has 40 carbon, 56 hydrogen and no oxygen atoms.

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- (2) All are soluble in fats and fat solvents, and insoluble in water.
- (3) All are unchanged by heat, acids and alkalis, but are sensitive to light, and tend to absorb oxygen from the air, that is, to *oxidize*. Oxidation destroys potency.
- (4) The provitamins are bright yellow, while the A₁ and A₂ forms are nearly colorless.

What do the vitamins A do?

- (1) They are essential for *clear vision* and they prevent *night blindness*.
- (2) They are essential for maintaining *resistance* to germs and infection of the covering and lining membranes of the body (skin, linings of stomach, windpipe, nose, eyelids, etc.). These membranes are called *epithelial* tissues.
- (3) They are essential to the proper formation of tooth enamel.
- (4) They promote and are necessary for growth.

How do they accomplish these effects?

(1) Vision

The picture formed by light rays on the retina of the eye is *developed* (like a photograph) by nerve impulses which travel from the retina over

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the optic nerve to the brain, where they are translated into vision. These nerve impulses are caused by *chemical changes* involving a pigment in the retina called *visual purple* (rhodopsin).

Light rays acting on visual purple *bleach* it to a yellow substance called *retinene*. This bleaching produces the nerve impulses. Once it is bleached, this pigment cannot again respond to light until it has been *changed back* to visual purple. It is in this *regeneration* of retinene to visual purple that vitamin A functions. No regeneration can take place without it. Vitamin A is also essential to the regeneration of another retinal pigment known as visual violet.

(2) Resistance to infection

(a) *Nose and Mouth*

Layers of cells covering various parts of the body, both inside and outside, are called *epithelial tissues*. Change in the structure of these tissues is caused by too little supply of vitamin A, and is known as *metaplasia*. In animals, lack of vitamin A results in loss of the ability to keep these tissues in healthy condition.

The most important result of the change in tissue structure is that the surface affected *no longer performs its function of protecting the*

VITAMIN A

area from the attack of germs and infection. The question of whether infection occurs or not depends on how accessible the area is to bacteria. For this reason epithelial changes of the nose, throat and mouth most often result in an infection.

Colds probably start with infection by a specific germ, accompanied by congestion of the nasal passage. Under these conditions it is easy for secondary infections to develop. The Council of Pharmacy of the American Medical Association states its viewpoint on the effectiveness of vitamin A in resisting colds as follows:

“Present indications are that vitamin A is an aid toward establishing resistance of the body to infections in general only when there has been a decrease in body reserves of the vitamin and the ingestion of vitamin A is inadequate. It has not been shown to be specific in the prevention of colds, influenza, and such infections, nor has it been demonstrated that ingestion of vitamin A far in excess of that necessary for normal body function, and readily obtained from a properly selected diet, is an aid in preventing various types of infections.”

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(b) *Skin*

The skin is one of the first tissues to show vitamin A deficiency. This is indicated by hardening of the lining of hair follicles, which results in their becoming plugged with masses of hardened material which interferes with the secretion of the oil glands of the skin. This causes skin dryness, which cannot be corrected merely by lubricating the skin tissue.

(c) *Genito-urinary tract*

Deficiency of vitamin A produces changes in the epithelial tissue of the uterus. As with the respiratory tract, this prepares the way for development of infection or change of function in this region.

There is little evidence to show that lack of vitamin A is the cause of bladder stones, although it has been claimed that such is the case.

(d) *Eye Regions*

The condition known as "dry-eye" (xerophthalmia) is related to Vitamin A deficiency, although it does not appear until the deficiency has continued for some time. It is characterized by hardening of the epithelial tissues of the eyeball and the under surface of the eyelid. The tear

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glands atrophy, so that tears cannot wash the eyeball, which becomes bloodshot and swollen. In extreme cases the eyeball may become ulcerated.

The fact that this was the first ailment found to be due to lack of vitamin A is responsible for the early use of the term "anti-dry-eye" or "anti-xerophthalmic" to describe this vitamin.

(3) Tooth Enamel

Tooth enamel is an epithelial structure. Lack of vitamin A causes metaplasia of the organs producing the enamel. This is followed by loss of enamel and exposure of the dentin, which gives the teeth a chalky appearance. At the same time tooth growth ceases. An adequate supply of vitamin A is therefore essential for proper formation and maintenance of tooth enamel.

How much Vitamin A do we need daily?

For the adult the *minimum* requirement appears to be about 4000 International Units daily. Amounts necessary not only to protect against pathological conditions but to insure adequate growth have been variously estimated. A recent estimate of vitamin A requirements given by the National Research Council's Committee on Foods and Nutrition is as follows:

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<i>Individuals</i>	<i>Calorie Intake</i>	<i>International Units Vitamin A Daily</i>
Man weighing 140 lbs.		
Moderately active...	3000	5000
Very active.....	4500	5000
Sedentary.....	2500	5000
Woman weighing 112 lbs.		
Moderately active...	2500	5000
Very active.....	3000	5000
Sedentary.....	2100	5000
During latter half preg-		
nancy.....	2500	6000
During lactation.....	3000	8000
Children up to 12 years		
Under 1 year.....	50 per lb.	1500
1- 3 years.....	1200	2000
4- 6 years.....	1600	2500
7- 9 years.....	2000	3500
10-12 years.....	2500	4500
Children over 12 years		
Girls		
13-15 years.....	2800	5000
16-20 years.....	2400	5000
Boys		
13-15 years.....	3200	5000
16-20 years.....	3800	6000

In its foreword to the publication of this table, the Committee stated:

“In using these recommendations it is important that the purposes and general policies which the Committee had in mind in formulating them should be understood:

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"The allowances for specific nutrients are intended to serve as a guide for planning adequate nutrition for the civilian population of the United States. The quantities as given were planned to provide a reasonable margin of safety, but they do not allow for any extensive losses in cooking. . . . The Committee realizes that the values proposed will need to be revised from time to time as more knowledge of nutritive requirements becomes available.

"It is understood that these allowances are for persons in health, and they may vary markedly in disease."

Where can we get Vitamin A?

Capsules, tablets, and fish liver oils or liver oil concentrates are everywhere available in drug stores today. In natural foods the following classification helps in choice:

Food Sources of Vitamin A and Provitamin A

<i>Type of Food</i>	<i>Excellent Sources</i>	<i>Good Sources</i>
Animal products	Fish liver oils, liver, fish roe, egg yolk, butter, cheese.	Cream, kidney, oysters, whole milk, red salmon.
Vegetables	Kale, spinach, dandelion greens, dock, escarole, chard, lambs-	Green asparagus, okra, Brussels sprouts.

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	quarters, turnip tops, green lettuce, col- lards, water cress, Chinese cabbage, broccoli, mustard greens, beet greens, carrots, sweet pota- toes, yellow squash, sweet peppers, red to- matoes, green peas, green beans.	globe arti- chokes, yellow tomatoes.
Fruits	Apricots, papayas, mangoes, prunes, yel- low peaches.	Avocados, gua- vas, cantaloups, black- berries, bana- nas, pineapples, black currants, blueberries, green and ripe olives, dates, deep-yellow juice oranges.
Cereal		Yellow corn meal.

For quantitative distribution of vitamin A in foods, see Appendix.

III. The B Complex

VITAMIN B₁ (THIAMINE)

Why is it called Vitamin B₁?

In 1916 a water extract of certain substances which were found to cure beri-beri and also to promote growth was defined as "water-soluble B." Later it was discovered that this extract contained not one, but several vitamins (the B complex). Although some of these had no effect on beri-beri, they did cure other ailments. It was therefore decided to restrict the term "vitamin B₁" to the factor that prevented beri-beri. The name "thiamine" applies to vitamin B₁, which is now produced synthetically. It is sold under the name of *thiamine chloride*.

What is Vitamin B₁?

Vitamin B₁, or thiamine, is a carbon-containing (organic) compound composed of two parts, one of which contains *nitrogen* and the other *sulfur*. Its richest sources in nature are yeast and the outer coating and germ of the kernels of wheat, corn, rice, rye, barley, etc. It also occurs

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in a slightly different form in the tissues of the human body.

What are the properties of Vitamin B₁?

The pure, or synthesized, form of B₁ is crystalline. This vitamin is not destroyed by absorbing oxygen, as some others are, but it is separated into its nitrogen and sulfur components by sulfite. This separation completely inactivates it.

Vitamin B₁ is *destroyed* by heating, especially above the boiling point of water (212° F.), if the exposure to heat goes on for some time, as in frying, roasting and baking. Pork chops may lose 35 per cent of their B₁ content during frying and roast beef up to 60 per cent.

Commercially prepared B₁ crystals have a slightly salty taste and are colorless and odorless. They take up water readily from the air and are very soluble in water, but only slightly soluble in alcohol.

How is Vitamin B₁ potency expressed?

As shown in the table on page 16, an International unit or a U.S.P. unit of vitamin B₁ is equivalent to .00333 milligram of B₁ crystals. A Sherman-Chase unit is about half an International unit, or .00166 milligram. Labels now usually express potency in milligrams or in Inter-

VITAMIN B₁

national or U.S.P. units. One milligram of B₁ contains 333 International units.

What does Vitamin B₁ do?

- (1) It is essential for utilization of starches and sugars (carbohydrates) by the body tissues.
- (2) It stimulates appetite and normal intestinal functions.
- (3) It is essential to proper nerve function.
- (4) It is necessary for reproduction and lactation.
- (5) It cures beri-beri and prevents certain forms of neuritis and the heart and circulation disorders associated with this disease.
- (6) It promotes and is essential to growth.

How does it accomplish these effects?

- (1) Utilization of starches and sugars (carbohydrates)

It was shown by Funk in 1914 that persons on a diet rich in sugars and starches showed symptoms of B₁ deficiency more quickly than those on diets rich in fats and proteins. This was the first indication that vitamin B₁ needs are related to body *fuel supply*, and to the special kind of fuel represented by *carbohydrates*.

Cowgill followed up this finding by working out a mathematical expression for minimum

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human requirements of vitamin B₁, that is, enough to prevent beri-beri. His formula was based on the weight and on the caloric intake. Using this formula, a 140-lb. man with an intake of 2500 calories would require 248 International units of vitamin B₁ daily.

The reason that vitamin B₁ can "handle" the sugars and starches in the body is that it is an *active chemical factor* in the transformation of glucose (sugar) into carbon dioxide and water, with release of *energy*. With too little B₁, the change is incomplete. This results in an accumulation of *pyruvic acid*; indeed the amount of this acid in the blood is used today as an indication of a lack of this vitamin.

This faulty or incomplete burning of fuel (sugars and starches) is *all that is necessary to explain abnormal nerve and tissue behavior* in cases of B₁ deficiency; with incomplete fuel utilization the ability of the tissue to work normally is hampered.

(2) Effect on appetite

Loss of appetite has always been associated with a deficiency of vitamin B₁. It was originally suggested that the reason for this lay in the lack of nerve stimulus to the muscles controlling movements of the stomach. Though it is defi-

VITAMIN B₁

nately known that weakness of the stomach muscles is a result of lack of vitamin B₁, it is not so certain that this is due to nerve derangement. The precise way in which B₁ deficiency causes loss of appetite is still uncertain.

(3) Other consequences of B₁ deficiency

(a) Constipation

That vitamin B₁ has a definite effect on the function of the intestines and that it corrects some types of constipation is generally agreed. It has been proved that the laxative effect of bran depends not only on its providing bulk, but on its B₁ content. The laxative action of mineral oil is increased by addition of crystalline vitamin B₁. There are various causes of constipation, and in any given case the test of its relation to B₁ deficiency is whether or not it responds to treatment with this vitamin.

(b) Heart effects

Since heart failure is the ultimate cause of death in beri-beri, which vitamin B₁ has been proved to cure, the question of the effect of B₁ on the heart has been studied by several investigators. However, no conclusive evidence has been established as to just what part this vitamin plays in this respect.

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(c) Nerve Effects

Vitamin B₁ has often been called the *morale* vitamin because of its effect on the nervous system. The mechanism of this effect has been explained on the basis that lack of this vitamin *prevents* normal metabolism of the nerve tissue. One of the striking effects of treating nervous derangements with vitamin B₁ is the promptness of recovery. Just how the vitamin produces this recovery or controls the behavior of nerve tissue is uncertain. One of the most sensational developments following the availability of pure thiamine has been the demonstration that the results of *excessive alcohol intake* are frequently identical with those of vitamin B₁ deficiency.

How much Vitamin B₁ do we need?

Cowgill's formula indicated that a 140-lb. man with a calorie requirement of 2500 needs at least 248 International units of B₁ daily. It should be emphasized that this is the minimum requirement. Six hundred units is not excessive for the best health conditions.

Experimentation on human subjects has shown that restriction of B₁ produces moodiness, sluggishness, indifference, fear and mental and physical fatigue, and that until the daily intake

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reached 600 International units per day full recovery and efficiency was not attained. Many nutritionists recommend at least 900 units per day (3 mgms).

The National Defense Research Council's recommendations (see p. 28) are as follows:

<i>Individual</i>	<i>Mgms. B₁</i>	<i>International Units Vitamin B₁ Daily</i>
Man		
Moderately active	1.8	599
Very active	2.3	766
Sedentary	1.5	500
Woman		
Moderately active	1.5	500
Very active	1.8	599
Sedentary	1.2	400
Latter half pregnancy	1.8	599
During lactation	2.3	766
Children up to 12 years		
Under 1 year	0.4	133
1- 3 years	0.6	200
4- 6 years	0.8	266
7- 9 years	1.0	333
10-12 years	1.2	400
Children over 12 years		
Girls		
13-15 years	1.4	466
16-20 years	1.2	400
Boys		
13-15 years	1.6	523
16-20 years	2.0	666

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Where can we get Vitamin B₁?

Synthetic thiamine or thiamine chloride is now available in pure form or in concentrates and tablets in all drug outlets. Yeast and liver preparations are rich in this factor as are also wheat germ and rice polishings and their extracts. The following table shows its relative distribution in foodstuffs:

Food Sources of Thiamine (Vitamin B₁)

<i>Type of Food</i>	<i>Excellent Sources</i>	<i>Good Sources</i>	<i>Fair Sources</i>
Animal prod- ucts	Lean pork, chicken, kid- ney, liver.	Egg yolk, brains, lean mutton, fish roe, codfish, sar- dines, whiting.	Fresh milk (whole or skim).
Vege- tables	Green peas, green lima beans.	Potatoes, sweet corn, sweet pota- toes, Brussels sprouts, cauli- flower, cabbage, mushrooms, spin- ach, turnip greens, water cress, garden cress, lettuce, col- lards, kale, on- ions, leeks, toma- toes, wax and green beans, pars- nips, beets, car- rots.	Turnips, broccoli, kohlrabi, eggplant.

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Fruits	Prunes, avocados, pineapples, or- anges, grapefruit, tangerines, dates, figs, plums, pears, apples, cantaloupes. Bananas, watermelons, raspberries, blackberries.
Seeds	Wheat germ, corn germ, rice polishings, wheat bran, oats, whole-grain wheat, rye, barley, brown rice, peanuts, soybeans, cowpeas, navy beans, dried peas. Hazelnuts, chestnuts, Brazil nuts, walnuts, almonds, pecans.

For quantitative distribution in foods, see Appendix.

IV. The B Complex

I. VITAMIN B₂ (RIBOFLAVIN)

The discovery that "water-soluble B" consisted of *several* vitamins was proved conclusively when the substance known as *riboflavin* was identified. In England this was called vitamin B₂, and in the United States it was called vitamin G; it is now universally referred to by its chemical name, riboflavin.

What is Riboflavin?

Riboflavin is found in various sources. It was first shown to be present in milk (1879), long before anything was known about vitamins. Later investigators (1925) described this form as *lactoflavin*. It has also been discovered in liver and called hepato-flavin, and in other substances. All these forms have been shown to be identical in chemical structure—a single type of sugar called *ribose*, combined with a yellow pigment (flavin). Combining the two words gives ribose-flavin, or riboflavin. This name now applies to vitamin B₂ regardless of where it occurs.

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What are the properties of Riboflavin?

Riboflavin is slightly soluble in water; it does not withstand the action of direct light, but is practically unaffected by heat. The pure substance is a light, yellow-colored, odorless powder containing seventeen carbon atoms, twenty hydrogen atoms, four nitrogen atoms and six oxygen atoms. In solution it shows a strong yellow-green fluorescence. It is insoluble in acetone, chloroform and ether, but somewhat soluble in alcohol. It is decomposed by visible and ultraviolet light.

How is Riboflavin potency expressed?

The United States Food and Drug Administration now requires that labels state the riboflavin potency in weight, that is, in milligrams or fractions of a milligram. A thousandth of a milligram is a microgram or one gamma (γ), and both terms (micrograms and gammas) are used on labels today.

Bourquin and Sherman worked out a method of determining the riboflavin content of food sources, and a value known as the "Sherman-Bourquin unit." This sometimes appears on labels. It may be converted to micrograms on the basis that one Sherman-Bourquin unit is equivalent to 2.5 micrograms of riboflavin (.0025 milligram).

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What does Riboflavin do?

- (1) It prevents cracking of the lips and of the angles of the mouth, and certain other facial lesions (cheilosis or cheilitis).
- (2) It prevents abnormal changes in the eyes, which if not prevented, may result in failing vision and cataract.
- (3) It promotes and is essential to health.
- (4) It helps us burn the body fuel to produce energy.

How does it accomplish these effects?

(1) Skin Lesions

It was found in 1938 that sores occurring in the corners of the lips, which had previously been known as *cheilitis* or *cheilosis*, were apparently a direct effect of riboflavin deficiency. On a diet of corn meal, cowpeas, lard, casein, white flour, white bread, calcium carbonate, tomato juice, cod liver oil, syrup and iodide of iron, Sebrell produced a whitening of the skin at the angles of the mouth. These areas soften, and in a few days surface cracks and fissures appear. These remain moist and become covered with a honey-colored crust which can be removed without causing bleeding.

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This condition is similar to that earlier found in children and called *perleche*. It immediately improved when treated with riboflavin. In 1939 it was definitely proved that cheilitis is cured by adequate dosage of riboflavin.

Deficiency of riboflavin in the diet of rats results in loss of hair and atrophy of the oil-secreting glands of the skin. Just how riboflavin corrects these conditions is not known.

(2) Effect on Vision

Cataract has been produced in rats by feeding them on diets lacking in riboflavin. This has been duplicated with other laboratory animals. The cataract was cured by treatment with synthetic riboflavin, which indicates that lack of this vitamin may be a definite cause of cataract.

It was also noted that the blood-vessels of the eyeball of rats were adversely affected by lack of riboflavin; indeed, this symptom preceded all others known to be due to riboflavin deficiency. This condition was rapidly cured by intake of riboflavin.

(3) Other Effects

It is possible that riboflavin may be a factor in curing pernicious anemia; it has an important general effect on growth, and may have some

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effect on the production of hemoglobin, or red blood corpuscles.

How much Riboflavin do we need?

The adult requirement has recently been set as probably three milligrams daily and at least 2 milligrams. The National Defense Research Council's allowances (see p. 28) are as follows:

	<i>Milli-grams of Riboflavin</i>	<i>Micro-grams or gamma</i>	<i>Sherman-Bourquin Units</i>
Man			
Moderately active	2.7	2700	1090
Very active	3.3	3300	1320
Sedentary	2.2	2200	880
Woman			
Moderately active	2.2	2200	880
Very active	2.7	2700	1090
Sedentary	1.8	1800	720
During latter half pregnancy	2.5	2500	1000
During lactation	3.0	3000	1200
Children under 12 years			
Under 1 year	0.6	600	240
1- 3 years	0.9	900	360
4- 6 years	1.2	1200	480
7- 9 years	1.5	1500	600
10-12 years	1.8	1800	720
Children over 12 years			
Girls			
13-15 years	2.0	2000	800
16-20 years	1.8	1800	720

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Boys

13-15 years.....	2.4	2400	960
16-20 years.....	3.0	3000	1200

Where can we get Riboflavin?

Like thiamine, riboflavin is now available in synthetic form in drug stores, and in capsules or concentrates. Its distribution in foods is shown in the following table:

Food Sources of Riboflavin

<i>Type of Food</i>	<i>Excellent Sources</i>	<i>Good Sources</i>	<i>Fair Sources</i>
Animal products	Liver, kidney, heart, lean muscle meats, eggs, cheese, dried (whole or skim), condensed, and evaporated milk.	Fresh (whole or skim) milk, buttermilk, whey.	
Vegetables	Turnip tops, beet tops, kale, mustard greens.	Peas, lima beans, spinach, water cress, collards, endive, broccoli, green lettuce, cabbage, cauliflower, carrots, beets.	
Fruits		Pears, avocados, prunes, mangoes, peaches.	Bananas, cured figs, grapefruit, oranges, apricots, guavas, papayas, muskmelons, apples.
Seeds	Germ portion of wheat, rice polishings, peanuts, soybeans.	Whole-grain wheat, dried legumes.	

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For quantitative distribution of Riboflavin in foodstuffs, see Appendix.

2. NICOTINIC ACID (VITAMIN P-P)

In 1937 still another vitamin was found in the prolific "water-soluble B." It was found to cure the tongue and skin inflammation associated with the disease called pellagra in humans, and "black-tongue" in dogs. This disease is especially prevalent in localities such as the South, where the very poor subsist on starvation rations.

What is Nicotinic Acid?

It is an organic, or carbon-containing, compound which was shown to be present in the product first isolated from rice polishings by Funk. However, it was considered to be merely an impurity, as it had no beneficial effect on beri-beri. It should be mentioned that it bears no relation, chemical or otherwise, to *nicotine*, in spite of the similarity of the names.

What are its properties?

Nicotinic acid is a so-called "carboxylic" acid, having six carbon, five hydrogen, one nitrogen, and two oxygen atoms.

It may be obtained as a white, odorless, crystalline powder melting at 235° C. It does not ab-

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sorb oxygen from the air (oxidize), and is not affected by heat. It is slightly soluble in water, and is soluble in alcohol.

How is Nicotinic Acid potency expressed?

In either milligrams or ounces.

What does Nicotinic Acid do?

It prevents and cures the sores, or *lesions*, as doctors call them, which are characteristic of pellagra in humans, and the analogous disease called blacktongue in dogs. Nicotinic acid amide is just as effective and is less irritating.

What is Pellagra?

Pellagra is a disease affecting the skin, alimentary tract and the central nervous system. The skin becomes rough, reddened, scaling, and cracked and is easy to distinguish from normal skin. These sores usually appear on the backs of the hands, the elbows, knees, ankles, neck, and underarm regions.

First to appear are lesions of the alimentary tract. Loss of appetite and burning of the tongue give way to intense inflammation of the tongue, mouth and gums. This is followed by stomach and intestinal inflammation. The changes in the

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nervous system may result in delusions and hallucinations.

The disease is aggravated by exposure to sunlight.

How does Nicotinic Acid correct Pellagra?

Probably by providing building material for the conduct of normal cell metabolism, and thus acting to keep tissues healthy. Nicotinic acid is therefore not a "specific," or direct, cure for skin inflammation, but is necessary to keep the skin and digestive tract tissues in healthy condition. It also provides material for the building of coenzymes used in tissue metabolism.

How much Nicotinic Acid do we need?

The adult requirement is at least ten milligrams daily. The suggested allowances of the National Defense Research Council (see p. 28) are as follows:

	<i>Milligrams Nicotinic Acid</i>
Man	
Moderately active	18
Very active	23
Sedentary	15
Woman	
Moderately active	15
Very active	18

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Sedentary	12
During latter half of pregnancy	18
During lactation	23
Children under 12 years	
Under 1 year	4
1- 3 years	6
4- 6 years	8
7- 9 years	10
10-12 years	12
Children over 12 years	
Girls	
13-15 years	14
16-20 years	12
Boys	
13-15 years	16
16-20 years	20

It must be pointed out, however, that those afflicted with pellagra are usually deficient in several other vitamins as well, especially A, C, B₂, and B₆, and frequently need an increased quantity of these vitamins together with nicotinic acid.

Where can we get Nicotinic Acid?

It is on sale in pure form in drug outlets or in combination with other vitamins in yeast and in capsules, tablets and concentrates. Its distribution in foods has not been sufficiently studied to provide comprehensive tables. Elvehjem has reported the following values:

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Nicotinic Acid Content of Foods

<i>Foodstuff</i>	<i>Mg. Nicotinic Acid per gm. dry material</i>	<i>Foodstuff</i>	<i>Mg. Nicotinic Acid per gm. dry material</i>
Liver, pork	1.2	Brain, beef	0.3-0.5
Liver, lamb	1.2	Heart, pork	0.3
Liver, veal	0.9	Heart, beef	0.3
Kidney, pork	0.85-1.0	Yeast, brewers'	1.0
Pork loin	0.45-0.6	Yeast, bakers'	0.5
Pork ham	0.4	Skim milk powder	0.05-0.15
Beef tongue	0.4-0.5	Wheat germ	0.05-0.10
Veal	0.5	Dried cereal grass	0.10-0.15

Sebrell has shown that the following foods contain significant amounts of the pellagra-preventive substances: Beef, chicken, pork, salmon, collards, kale, turnip greens, peas, beans, cabbage, cowpeas, mustard greens, spinach.

3. PYRIDOXINE (VITAMIN B₆)

In the search for other vitamins in the B complex it was found that a specific type of skin inflammation in rats resulted from lack of what was first called vitamin B₆, and is now known as *pyridoxine*. This vitamin was chemically identified at six laboratories in the same year.

What is Pyridoxine?

It is an organic compound made up of eight carbon, eleven hydrogen, two oxygen, and one

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nitrogen atom. It has been shown to correct certain symptoms of pellagrins which are not affected by nicotinic acid.

What are the properties of Pyridoxine?

It melts at 205° C., is not decomposed by acids, alkalies or heat; its crystals are salty tasting and water-soluble. In tissues, it probably exists in combination with a protein. It may also supply building materials for tissue cells.

How is Pyridoxine potency expressed?

The potency of this vitamin is expressed in terms of the amount necessary to cure the type of skin inflammation called *acrodynia* in rats within three weeks. It is generally considered that this unit is the equivalent of 0.1 milligram of pyridoxine crystals.

What does Pyridoxine do?

Very little is known as yet about the value of this vitamin in human nutrition. Its use in combination with B_1 and nicotinic acid in treating pellagrins has proved of definite value in correcting muscular fatigue. The human requirement and its exact function in human nutrition are not known.

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Where can we get Pyridoxine?

The distribution of pyridoxine in common foods has been reported by Schneider and others (1939) as follows:

<i>Food</i>	<i>Units per 100 gm.</i>	<i>Food</i>	<i>Units per 100 gm.</i>
Lettuce.....	25	Soybeans.....	400
Spinach.....	66	Cornmeal.....	400
Tomato.....	25	Wholewheat bread.	400
Potato.....	40	Oatmeal.....	330
Carrot.....	25	Flaxseed.....	1000
Beet.....	13	Rice polish.....	500
Banana.....	66	Wheat germ.....	1250
Orange.....	16	Beef tallow.....	330
Apple.....	25	Butter fat.....	200
Egg yolk.....	2500	Lard.....	2500
Milk, whole.....	40	Linseed oil (comm.)	2500
Milk, skim.....	14	Linseed oil (crude).	2500
Cheese, Cheddar..	250	Peanut oil.....	5000
Beef muscle.....	125	(ether extract)	
(raw, dried)		Peanut oil.....	5000
Beef muscle.....	125	(benzine extract)	
(roasted, dried)		Peanut oil (crude).	2500
Haddock, dried...	200	Rice oil (comm.)..	2500
Pork liver, dried..	500	Rice oil.....	5000
Alfalfa leaves.....	600	(ether extract)	
Beans, navy.....	400	Soybean oil.....	1000-
Peanuts.....	1660	(ether extract)	7000
		Wheat germ oil....	25000
		(comm.)	
		Wheat germ oil....	15000
		(ether extract)	
		Corn oil (comm.)..	20000
		Dried yeast.....	400

N.B. A unit equals the amount necessary to cure moderately severe acrodynia in 3 weeks.

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4. PANTOTHENIC ACID (FILTRATE FACTOR)

In 1939 R. J. Williams reported that he had isolated a compound which he called calcium pantothenate, the name being taken from the Greek meaning "from everywhere." This substance is universally distributed in *all living cells*. Of it Williams wrote:

"Since its discovery pantothenic acid has been found to be not only present in widely different tissues and organisms but to function as a potent physiological substance stimulating the growth of yeasts, molds, lactic acid bacteria, diphtheria bacillus, protozoa, young alfalfa seedlings and liver worts, and to stimulate the respiration of various tissues.

"There is evidence that the same substance is required by pigs and dogs and the inference is not a wild one that it is necessary for the nutrition of all the higher forms of animal life and that it makes up an essential part of every living cell."

What is Pantothenic Acid?

It is an organic compound, the commercial form of which is made up of one calcium, 16 carbon, 32 hydrogen, 2 nitrogen and 10 oxygen atoms. Its value in human nutrition has not yet

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been established. It is sometimes called "filtrate factor" because it was originally found in the residue of liver extract from which vitamins B₁ and B₂ had been removed by *filtration*. In the literature of nutrition, the word *factor* is often equivalent to *vitamin*.

What are its properties?

It is colorless, readily soluble in water and does not form crystals. The calcium salt has been synthesized. The acid itself is unstable. The salt, calcium pantothenate, is stable and is available in pure form.

How is its potency expressed?

With the availability of the calcium salt (calcium pantothenate) potency can now be expressed in terms of the actual weight of that substance.

What does Pantothenic Acid do?

It is not yet known how much is essential in human diet or exactly what it does. It has been found that the blood content of persons having pellagra contains less pantothenic acid than that of normal individuals, and that injection of pantothenic acid into the blood causes increase of *riboflavin* in the blood as well as of panto-

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thenic acid, with no other change in diet. It appears to be essential to human nutrition and is probably associated with distribution of riboflavin.

It is at least one of the factors which can prevent graying of the hair. Two substances have been isolated from the B complex to date which seem to be concerned with hair pigmentation, namely pantothenic acid and para-amino-benzoic acid. Wooley also claims that inositol is involved in hair growth. The theory of the part played by pantothenic acid and para-amino-benzoic acid in the coloring of hair is as follows to date: Pantothenic acid deficiency results in adrenal hemorrhage, which interferes with the pigment control of the adrenal gland. Para-amino-benzoic acid is concerned in the actual formation of coloring matter (melanins).

Where can we get Pantothenic Acid?

The commercial form (the calcium salt) is now available in drug stores. As its name indicates it is widely distributed in foods. Some sources are: peanut, soybean and cottonseed meal. Yeast, rice, bran, and alfalfa are rich sources. Beef, fish, and eggs contain it to some extent; vegetables like carrots, onions, peas and beans have been proved to supply it.

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5. OTHER MEMBERS OF THE B COMPLEX

The B complex vitamins so far described have been successfully isolated and their structure determined and confirmed by synthesis. The following members of the B complex are thought to exist, but their identity has not yet been proved.

(a) Vitamin B₈

In 1928 it was found that, when pigeons are fed on polished rice and water to produce symptoms of polyneuritis, the addition of concentrated solutions of B₁ corrects the neuritic symptoms but fails to restore the birds to normal weight. Air-dried yeast was found to be quite effective in this respect. Tests led investigators to assume the existence of a heat-destructible factor in yeast other than B₁ and B₂. The B-complex was thus considered to be of a "tripartite" nature, the third member being called vitamin B₃. It was recently suggested B₃ may be identical with pantothenic acid.

(b) Vitamin B₄

A heat-destructible, water-soluble factor different from B₁, B₂, or B₃, which prevented a sort of paralysis in rats, was reported in 1930. Its ex-

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istence has been confirmed, and it has been concentrated from yeast extracts and defatted liver. It is designated as B₄. Human need for it has not been demonstrated, but it is apparently required by chicks as well as by rats.

(c) Vitamin B₅

That pigeons require for prevention of weight loss a heat-stable factor other than B₂ led investigators to assume the existence of a vitamin B₅. This provided only weight *maintenance* of the pigeon; B₅ was necessary for weight *increase*. This is all that is known at present about this factor, with the exception of a recent suggestion that it may be identical with vitamin B₆.

(d) Vitamin B₇ (I)

Centanni (1935) claims to have isolated from alcohol extract of rice polishings a substance which was without effect on beri-beri or polyneuritis, but which did prevent digestive disturbances in birds.

(e) Vitamin H (Biotin)

It has been reported that a type of skin inflammation produced in rats by eating raw egg-white is cured by injecting a substance obtained from

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liver extract. This product was further concentrated and used effectively in doses of 3 to 5 micrograms. Its discoverer called it vitamin H. In 1936 a crystalline product, for which the name "biotin" was suggested, was isolated from egg-yolk. Previously a factor essential for the respiration of certain lower organisms had been found, to which the name "coenzyme R" was applied.

These three discoveries now appear to be dealing with the same substance. Since biotin has been obtained in crystalline form, it should be possible to determine definitely whether it is the same as vitamin H; if so, this joins the group of vitamins successfully identified.

(f) Vitamin J

Von Euler in 1935 reported the extraction of a factor from the juice of fruits that did not prevent scurvy but protected guinea pigs from pneumonia. This he called vitamin J. Its value in treating human pneumonia has not been demonstrated.

(g) Factors L_1 and L_2

Substances which are necessary to *milk formation* are said to be obtained from beef liver (L_1) and baker's yeast (L_2). They are thought to

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function in the maturation of the milk-producing tissues.

(h) Factor M

It has been found that nicotinic acid is of no value in correcting pellagra symptoms in the Rhesus monkey. Combinations of B₁, B₂, and nicotinic acid do not correct the mouth lesions. Dried brewer's yeast and liver extract do clear up the symptoms, however. A vitamin designated as Factor M has therefore been assumed to exist.

(i) Factor U

This is a vitamin apparently essential for chick growth. It is soluble in 50 per cent alcohol but insoluble in ether, acetone and isopropyl alcohol. Like W, its significance in human nutrition is unknown.

(j) Factor W

An additional rat growth promoting factor has been assumed and provisionally called Factor W. It may possibly be related to pyridine.

(k) Grass Juice Factor

The existence of a vitamin or vitamins in grass juice has been assumed, the nature of which has not yet been established. (This is not to be con-

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fused with the fact that many of the known vitamins are present in grass).

In view of the fact that the B complex consists of several vitamins and that deficiencies are usually multiple, B complex preparations are extensively used today to insure the presence of all the factors rather than relying on B₁, B₂, B₆, Nicotinic or Pantothenic acid alone. Such preparations are furnished by yeast, liver, wheat germ, rice polish or their extracts.

V. Vitamin C (The Antiscurvy Vitamin)

What forms exist?

This vitamin is what chemists call a sugar acid. There are at least four forms which are more or less active in preventing scurvy, but the most potent and most widely distributed form is ascorbic acid. When we speak of pure vitamin C, it is ascorbic acid we have in mind.

What are the properties of Vitamin C?

Ascorbic acid is a white, crystalline product now available in pure form as tablets which remain quite stable in the dry state. It is readily soluble in water but insoluble in oils, chloroform or ether. It is soluble in alcohol. One milligram of pure ascorbic acid is equivalent to 20 International units.

In solutions, particularly alkaline ones, ascorbic acid *oxidizes* and gradually loses its activity. Thus addition of baking soda to peas during cooking, while it improves their color, helps to lower their vitamin C content. Oxidation is stimulated by exposure to light and air. Heat alone does not seriously damage the substance, but

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when it is in contact with air at the same time, heat accelerates the oxidation, and resulting destruction of the vitamin activity is quite rapid. Keeping sources of vitamin C at low temperatures therefore helps to retain their potency. Tressler and associates have reported the following experiments with spinach; note how much greater is the rate of loss of ascorbic acid at the higher temperature:

<i>Variety of Spinach</i>	<i>Temperature of Storage</i>	<i>Milligrams of active ascorbic acid in one gram of leaves after</i>			
		<i>0 days</i>	<i>3 days</i>	<i>7 days</i>	<i>17 days</i>
Hollandia	34-37° F.	.79	.76	.64	0.49
Hollandia	73-79° F.	.79	.39	.03	0.00

The destruction due to oxidation proceeds in two steps:

- (a) Conversion of ascorbic acid to dehydro-ascorbic acid. This reaction is reversible and the body can utilize either acid.
- (b) Oxidation of dehydro-ascorbic to threonic and oxalic acids. This reaction is *not* reversible and the body cannot convert these acids to antiscorvy material.

The ease with which the activity of ascorbic acid is destroyed by oxygen makes its retention in active form in foodstuffs a problem of consid-

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erable care in storage, cooking, canning, and dehydration processes.

How is Vitamin C potency determined?

In 1932 it was shown that the presence and amount of ascorbic acid in a solution could be determined by using a dye known as phenol-indo-phenol. That procedure is now the basis of *colorimetric* determinations. Its presence and amount can also be determined by measuring the quantities of source necessary to prevent or cure scurvy in guinea pigs. As stated above, the International unit of anti-scorbutic vitamin is now set as .05 milligram calculated at 20 units per milligram.

What does Vitamin C do?

The outstanding symptom of scurvy is *hemorrhage*. Bleeding caused by weakness of the blood vessels results from vitamin C deficiency. Such bleeding may occur in various parts of the body, and disturbance of function by it causes the joint, gum, and gastro-intestinal indications of vitamin C deficiency, or scurvy. Its lack also results in faulty formation of the dentine of teeth and of bone. Lack of C is also believed to be responsible for certain disturbances of tissue metabolism.

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Vitamin C is thought to be capable of overcoming the toxic substances produced by certain bacteria such as diphtheria.

How does Vitamin C produce these effects?

(1) Failure of Intercellular Substance

It will be recalled that lack of vitamin A results in metaplasia of the surface, or epithelial tissues, and that vitamin A provides something needed *within the epithelial cell* for its normal form and behavior. The hemorrhage and tissue changes of scurvy are due to lack of something essential to the normal function and behavior of *intercellular* (between cell) materials, especially those associated with the *connective* tissues. Under normal conditions a typical cell (the fibroblast) lies in an amorphous *intercellular* substance within which fibrils are formed; these in turn become cemented together in wavy bands of collagen (a glue-like substance) like the setting of a gel. In guinea pigs deprived of vitamin C the fibroblasts are present just as in healthy pigs, but fibrils and collagen fail to form. With adequate dosage of vitamin C these intercellular substances appear within 18 hours.

In bone, the functioning cells are called *osteoblasts*, and the intercellular substance is bone-forming tissue. In the teeth the cells are

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known as *odontoblasts*, and the intercellular substance is dentine. In both bones and teeth, lack of adequate vitamin C affects the character of the intercellular substance. Supplying vitamin C quickly restores it to normal.

Weakness of the blood vessels and consequent bleeding are therefore believed to be due to failure to supply "cement" material to the vessel wall. Faulty dentine formation in teeth results from lack of an essential substance required by the tooth odontoblasts. In bones, the condition suggests that in the absence of vitamin C the osteoblasts, being unable to form bony tissue, revert to their primitive connective tissue form and try to set up a fibrous union. This is revealed by x-ray and is a means of diagnosing vitamin C deficiency.

Some of these changes in bone are strikingly like the changes that occur in rickets, and it is often difficult to determine whether the deficiency is one of vitamin C or vitamin D, especially when scurvy is complicated with rickets as often happens in infants.

(2) Vitamin C and Pyorrhea

There has been recent evidence of a direct relation between vitamin C and pyorrhea. The loosening of teeth in scurvy by both man and

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animals has been frequently observed. There may be two types of pyorrhea; one is a local inflammatory disease, the other a systemic process causing atrophy of the alveolar bone (jaw bone). The latter is similar to the conditions found in guinea pigs on a C-deficient diet; and in a limited number of patients with this type of pyorrhea there was a correlation between lack of ascorbic acid in the blood and weakening of the alveolar bone. Too little vitamin C in the diet may be therefore an important factor in producing this type of pyorrhea.

Abt and Farmer (1938) summarize the tooth situation as follows:

“Although there is still a dearth of exact knowledge of vitamin C in its relation to dental diseases in man, there is a general unanimity of opinion that an adequate intake of vitamin C is necessary for normal tooth growth and tooth structure, and the maintenance of healthy gums in man.”

(3) Blood Changes Due to C Deficiency

Vitamin C may also affect the constituents of the blood. For example, it is claimed that vitamin C accelerates the coagulation time of rabbit's blood, and that the coagulation time of human blood is shortened in hemorrhagic cases and pro-

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longed in normal persons. The white cells are said to carry a greater quantity of vitamin C than either the plasma or the red cells, and it has been suggested that vitamin C has a direct relation to the number of circulating white cells.

In scurvy there is usually a moderate degree of anemia, and it has been shown that vitamin C is beneficial in some of these cases when iron and liver extracts are ineffectual.

(4) Relation to Infection

There are a good many observations indicating that the presence of infection creates an increased demand for vitamin C, that vitamin C may be destroyed in the body by the action of infecting organisms, and that it may be helpful in controlling the immune bodies used to combat infections. But the exact way in which the vitamin functions is still undetermined.

How much Vitamin C do we need?

Abt and Farmer have worked out blood tests for C content and have reached conclusions as to what condition means inadequacy, borderline state, and sufficiency. According to them, if the blood plasma content of ascorbic acid falls below 0.5 mg. per 100 cc. the individual may be considered liable to scurvy. If the blood content is

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1 mg. per 100 cc. or more, the intake and absorption may be considered normal and adequate. Values between 0.5 and 1 mg. per cent are borderline cases suggesting need for increased vitamin C.

The National Defense Research Council's allowances (see p. 28) are as follows:

	<i>Milligrams Ascorbic Acid</i>	<i>International Units</i>
Man		
Moderately active	75	1500
Very active	75	1500
Sedentary	75	1500
Woman		
Moderately active	70	1400
Very active	70	1400
Sedentary	70	1400
During latter half of pregnancy .	100	2000
During lactation	150	3000
Children under 12 years		
Under 1 year	30	600
1- 3 years	35	700
4- 6 years	50	1000
7- 9 years	60	1200
10-12 years	75	1500
Children over 12 years		
Girls		
13-15 years	80	1600
16-20 years	80	1600
Boys		
13-15 years	90	1800
16-20 years	100	2000

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Where can we get Vitamin C?

Citrus fruits, tomatoes and vegetable greens are recognized today as our richest natural source of this factor. As the vitamin is producible synthetically without loss of potency as compared with natural sources it is of course available in tablets, capsules and concentrates. The following list is suggestive:

<i>Type of Food</i>	<i>Excellent Sources</i>	<i>Good Sources</i>
Animal products	Liver, brain.	Kidney.
Vegetables	Collards, turnip greens, mustard greens, kale, watercress, spinach, dandelion greens, sweet peppers, kohlrabi, rutabagas, turnips, Brussels sprouts, cauliflower, cabbage, broccoli, asparagus, fresh and canned tomatoes, green peas, corn, salad, radishes.	Endive, cucumbers, potatoes, sweet-potatoes, green beans, parsnips, rhubarb, leeks, onions, globe artichokes.
Fruits	Guavas, mangoes, oranges, lemons, grapefruit, tangerines, currants, strawberries, gooseberries, raspberries, cantaloupes.	Pineapples, cherries, cranberries, papayas, bananas, peaches, apples, avocados, watermelon.
Seeds	Sprouted seeds.	

VI. Vitamin D (The Antirickets Vitamin)

How many forms exist?

Of nine forms of vitamin D, all showing some degree of rickets-preventing action, two, D₂ and D₃, are most used today in concentrates, tablets and reinforcement of foodstuffs. D₃ appears to be the form most abundant in fish-liver oils and also the form which is activated by exposing human skin to ultraviolet light. D₂ is the form present in irradiated yeast and in the commercial product known as *Viosterol*. There is no D₁ for the reason that what was originally so named proved later to be a mixture.

For protection of chicks and poultry from rickets, D₃ seems to be superior to D₂, but for human use these two forms are approximately equivalent, unit for unit. The presence of other factors in natural sources, however, has considerable bearing on the amounts effective.

What are their properties?

Vitamin D₂ (activated ergosterol or calciferol). *Ergosterol* (or ergot sterol) is an *alcohol* found originally as the name indicates, in ergot.

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It is present in other fungi and abundantly in yeast. Few natural foods contain it in any significant amounts.

Ergosterol itself, which can be extracted as a white, odorless substance from yeast, ergot or other source, has no potency against rickets. To make it active in curing rickets, some *chemical change* induced by irradiation with certain kinds of light is necessary. Ergosterol, then, is a *pro-vitamin*. Vitamin D₂, or calciferol, is ergosterol *activated* with ultraviolet light. It is possible to activate ergosterol in other ways, such as with cathode rays and radium emanations, but ultraviolet light is most effective. The word *calciferol* was coined to define *activated ergosterol*, and an International unit of calciferol or D₂ is .000025 milligram of calciferol.

Viosterol is a solution of calciferol in oil, and is defined by the U. S. Pharmacopeia as a solution containing at least 10000 International units of vitamin D per gram.

Vitamin D₃, 7-dehydro-cholesterol, like D₂ is a sterol or alcohol; it also requires irradiation to activate it. Its unit is the amount necessary by rat bioassay test to produce the antiricketic action of .000025 mgm. of D₂ or calciferol. As stated above, it appears to be the form most abun-

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dant in fish-liver oils, though these may contain other forms of antiricketic substance.

These sterols have certain characteristics in common, namely, solubility in fats and fat solvents and insolubility in water. They are similar in elementary chemical composition. To date, the most important differentiation has been between D_2 and D_3 in behavior toward chicks and humans. D_4 may be the form present in cereals which is activated when these cereals are irradiated.

They do not change readily when once activated, and are quite resistant to the processes of food preservation and cooking.

How is potency determined?

To date we have no satisfactory chemical or physical test for vitamin D content and are forced to rely on a bioassay method which measures the amounts necessary to cure a ricketic condition in the test animal, either rat or chick. Such methods are specifically defined in the U. S. Pharmacopeia and in the A.O.A.C. methods.

What do Vitamins D do?

(1) Regulation of minerals in blood

Primarily they control the proper *distribution* of calcium and phosphorus in blood and tissues.

VITAMIN D

Vitamins D alone, then, without adequate intake of these minerals, will not be effective. But if the minerals are present in sufficient amount, the D vitamins will prevent rickets and certain phases of tooth decay and regulate our use of these minerals in all parts of the body.

(2) Arthritis

Reed and associates (1939) have studied the effect of high dosage of vitamin D on arthritis. The response has been favorable in some cases but not in all. We cannot at present, therefore, feel sure that vitamin D has a specific relation to the arthritic condition.

How do they accomplish this effect?

One of the earliest signs by which doctors detect rickets is the change in inorganic phosphate (a phosphorus compound) in the blood. This decreases appreciably in rickets and is restored to normal by vitamin D. Calcium content of the blood is also lowered in rickets and raised by vitamin D, but not to the extent of inorganic phosphate.

These changes in the mineral content of the blood suggest that rickets in some way *decreases* the absorption of *phosphorus* from the digestive tract into the blood and that vitamin D *increases* such absorption.

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Another sign of rickets is increase in the enzyme *phosphatase* in the blood. This enzyme occurs in various tissues of the body and is able to break down certain organic phosphoric acid combinations or esters. It has been shown that the cells concerned with bone growth and maintenance contain a high concentration of this enzyme. In rickets the addition of vitamin D *eliminates* phosphatase from the blood and concentrates it in the bone, where it is needed to cause precipitation of bone salt, calcium phosphate. Another way of expressing this effect is to say that it prevents leakage of phosphatase from the bone tissues.

Other possible values of Vitamins D

Vitamin D has been definitely shown to correct the morbid softening of the bone and the "bone hunger" of adults. During pregnancy it has the ability to prevent loss of calcium from the bones and teeth; and evidence has been produced to show that it is at least one factor in the prevention of tooth decay. It has also been claimed that vitamin D aids in fighting infection, but at the present time there is little to support this view.

The National Defense Research Council (see p. 28) recommends these daily intakes of calcium and vitamin D as desirable:

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	<i>Grams of Calcium</i>	<i>International Units Vitamin D</i>
Man		
Moderately active	0.8	400-800
Very active	0.8	400-800
Sedentary	0.8	400-800
Woman		
Moderately active	0.8	400-800
Very active	0.8	400-800
Sedentary	0.8	400-800
During latter half pregnancy . .	1.5	400-800
During lactation	2.0	400-800
Children under 12 years		
Under 1 year	1.0	400-800
1- 3 years	1.0	400-800
4- 6 years	1.0	400-800
7- 9 years	1.0	400-800
10-12 years	1.2	400-800
Children over 12 years		
Girls		
13-15 years	1.3	400-800
16-20 years	1.0	400-800
Boys		
13-15 years	1.4	400-800
16-20 years	1.4	400-800

How much do we need?

Jeans put the minimum human requirement from infancy to old age at probably 300 to 400 International units per day. Infants have, how-

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ever, been protected against rickets on as low as 120-130 units per day, especially when the vitamin is combined with milk. In pregnancy the need is temporarily increased and 800 units per day is recommended. Since we can produce vitamin D for body needs by exposing the skin to ultraviolet light or direct sunlight, the intake by mouth requirement will vary with the extent to which this is done. For distribution see the table in the Appendix.

How can we get it?

The human skin produces *provitamin D₃*. Therefore, when the skin is exposed to sunlight, which contains ultraviolet rays, this vitamin becomes active and is absorbed from the skin into the blood stream. Thus one way to get vitamin D is to take sun baths or to use lamps that produce ultraviolet rays. Remember that sunlight that passes through ordinary window glass is ineffective, as the glass filters out the activating ultraviolet rays. For the same reason the sunlight that passes through a smoky atmosphere is also ineffective.

Special types of window glasses which permit most of the ultraviolet rays to pass through make irradiation possible without exposure to the

VITAMIN D

weather; and there are various forms of ultra-violet lamps for use in indoor light-bathing.

Few foods contain enough vitamins D to be of value unless they have been *fortified* with vitamin concentrates; some such are now available, for example milk, margarines, and cereals.

Fish-liver oils are good sources and irradiated yeast is also rich in the D vitamins. These are available in capsules and other drug supply forms.

VII. Vitamin E (The Fertility Vitamin)

How many forms exist?

There are at least three substances which have vitamin E effect but the most potent one is known as *alpha-tocopherol*. The name is derived from "tokos," meaning "childbirth," and "phero," meaning "to bear." The "ol" termination indicates that it is an alcohol.

What are its properties?

Like other vitamins it is an organic compound which contains 29 carbon, 50 hydrogen and two oxygen atoms. It has two characteristic properties, ability to maintain *fertility* and ability to act as an *antioxidant*, that is, to retard oxidation. Because of the latter property it is extensively used today in capsulated vitamin products to protect *other* vitamins such as A and C from destruction by oxygen.

Vitamin E is fat-soluble and may be extracted from its natural sources by ether and other fat solvents. It is not changed by heat and light, but in the presence of ferric chloride or certain fats

VITAMIN E

it undergoes destruction. It is suggested that the damage to certain animals on a cod liver oil intake is due, not to the toxicity of the oil, but to its destructive action on the vitamin E of the ration fed. The antioxidant property appears to be independent of the fertility function.

Vitamin E is not affected by *visible* light but long exposure to ultraviolet (invisible) destroys it. It is unchanged by the action of enzymes, by atmospheric oxygen, by strong acids, and by hydrogenation. Drying and cooking operations do not inactivate it.

How is potency determined?

Several chemical methods have been proposed for estimating E potency but none has proved fully satisfactory as yet.

Potency is usually expressed in Evans units. An Evans unit is the amount of source or vitamin necessary in daily doses during the 21 days of gestation of a rat to insure production of healthy young; for example, an Evans 525 mgm. wheat germ oil is one which when fed in 25 mgm. doses per day for 21 days is just sufficient to insure birth of a live rat litter. This appears to be the equivalent of from 1 to 3 mgms. of pure alpha-tocopherol.

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What does Vitamin E do?

- (1) In addition to being essential to growth, this vitamin makes it possible for females to develop young to normal birth.
- (2) It prevents development of sterility in males. It has also been proved to prevent a form of muscular derangement called *dystrophy*.
- (3) It is claimed to prevent habitual abortion.

How does it accomplish these effects?

It was found that rats reared on diets otherwise complete but *lacking* some fat-soluble vitamin did not have offspring, though they were apparently normal in other respects. The females failed to carry their young to term; embryos died and were resorbed, but the female reproductive mechanisms were not damaged since adequate doses of the vitamin restored fertility. Male animals deprived of this factor, however, became infertile through degeneration of the germinal epithelium. Vitamin E dosage prevented this condition, but was ineffective in restoring them once the degeneration had occurred. Vitamin E can be destroyed by oxidation.

The role of vitamin E in the reproduction of rats has been fully established. It is essential, as stated above, for the production of normal litters

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by the female and to prevent sterility in the male. We have very little data to determine whether these results with rats can be duplicated in other animals. Large doses of wheat germ oil are said to increase the size of rabbit litters, and several investigators have reported that the hatchability of hen's eggs depends to a degree on the vitamin E content of the egg and the vitamin E diet of the hen. From studies of the effect of vitamin E on male fowl, it is evident that it is probably intimately associated with the behavior of the nucleus during cell division. The striking difference in response to vitamin E deficiency in male and female animals would appear to be that in the male the damage is done to part of the animal's own tissue, while in the female the damage is to the fetus and not to the female's own tissue. Several investigators have shown that a derangement of the muscles occurs in rabbits on a diet lacking in E, and that subsequent feeding of this vitamin cures this condition.

In human experimentation previous to the discovery of its possible relation to muscular dystrophy, the principal interest has been in prevention of abortion. Various investigators have reported success in the use of vitamin E for this purpose.

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How much do we need daily?

At the present time there exists no evidence to indicate a general deficiency of vitamin E in the American diet. It appears to be quite widely distributed in natural foodstuffs. For that reason, the Council of Pharmacy of the American Medical Association declined to allow claims of benefit from pharmaceutical preparations of this product.

Where can we get it?

Wheat germ oil is the richest natural source yet discovered. It has also been shown to be plentiful in animal foods such as milk, eggs, muscular portions of meat and fish and in the following vegetable foods: lettuce, spinach, watercress, legumes, peanuts, molasses, corn, wheat and many other whole grains.

VIII. Vitamin K (The Coagulation Vitamin)

How many forms exist?

Two forms have been isolated from natural sources. They are known as K_1 and K_2 . Both of these have been shown to be composed of a basic substance known as 1.4-naphthoquinone; a similar substance has been produced synthetically and has proved quite as effective as the natural products. Some of these synthetic forms have proved of great value because, unlike the natural forms, they are water-soluble and can therefore be used in injection treatments, as they are readily absorbed by the blood.

What are its properties?

Basically the vitamins K contain what chemists call the *quinone* group. Pure quinone is a yellow compound soluble in hot water, alcohol, and ether. There are many compounds formed from the quinone nucleus, and the ones that show anti-hemorrhagic qualities are grouped together as vitamins K. Each form has particular properties, and they range from products totally insoluble in water but soluble in fat solvents to forms easily

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soluble in water. K_1 was isolated from alfalfa, K_2 from putrefied fish meal. It is apparently producible by certain types of bacteria and may be formed in the human gut to some extent.

How is potency determined?

Several units are employed to express vitamin K potency. The Dam unit is described as follows:

“The Dam unit is the least amount per gram of a chick’s body weight which is necessary to prevent prolongation of blood clotting time beyond normal limits during a 2 week assay period.”

A clotting time of 1 minute was considered normal. Later a curative method was devised and in human studies the effect of K was measured by a test devised by Quick (1938). This method actually estimates the prothrombin content of the blood.

The Ansbacher unit is the minimum amount necessary to render the blood clotting time of a vitamin K-deficient chick weighing 70-100 gms. normal within 6 hours after taking. Synthetic vitamin K was found by this method to contain 2,000,000 Ansbacher units per gram.

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What does Vitamin K do?

Vitamin K normalizes the clotting power of the blood. It accomplishes this by control of the production of *prothrombin* in the blood. In this way it prevents certain types of hemorrhage.

How does it accomplish this effect?

The first to recognize the existence of vitamin K was Dam of Copenhagen (1935), though other workers had noted that chicks fed on ether-extracted fish meal showed 50 per cent of deaths due to bleeding.

Dam noted this same bleeding phenomenon and also that it could be controlled by giving the sterol-free portion of hog liver fat, or by feeding alfalfa. Because the unknown factor controlled the amount of prothrombin in blood and thus aided coagulation, Dam called it the *Koagulation* vitamin or vitamin K.

There are various theories of blood coagulation, but in general it is agreed that the clot is formed by the conversion of fibrinogen to fibrin by a ferment called *thrombin*. Thrombin does not exist ready-formed in circulating blood, but in a *prothrombin* state. This prothrombin is converted into thrombin by combination with calcium and by the action of a blood substance

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called *thromboplastein*. Blood clotting therefore proceeds in two steps:

- (1) Prothrombin + thromboplastein + calcium = thrombin.
- (2) Fibrinogen + thrombin = fibrin.

On the assumption that the blood clotting rate is proportional to the concentration of thrombin, Quick developed a method of making clotting time an actual *measure* of the prothrombin content of blood. As the effect of vitamin K is to *increase* blood prothrombin content, Quick's test is now in general use clinically to estimate the effect of vitamin K preparations on the prothrombin content of human blood. Prothrombin is believed to be formed in the liver. It is therefore obvious that if vitamin K is deficient in amount or if it is not absorbed into the blood, prothrombin production fails, blood clotting ability is lowered, and hemorrhage may result.

It is not yet known whether vitamin K enters into the formation of prothrombin as a chemical constituent or merely keeps certain tissues in a state of activity essential to its formation.

IX. Vitamin P (Citrin or Eriodictiol)

What is the vitamin?

In 1936 Szent-Gyorgyi isolated a flavone glucoside complex (a sugar compound) from lemon juice and later from lemon peel, and called it *citrin*. Provisionally its active component is called vitamin P. In the crude P concentrate several compounds have been identified, namely hesperidin, eriodictiol, and a quercitrin-like flavone. Eriodictiol can be readily formed from hesperidin, and there is a tendency to consider this the active vitamin in the citrin complex, but this is not fully established.

What are its properties?

Citrin, as isolated, forms light-yellow crystals sparingly soluble in water but very soluble in alkali, giving intense yellow solutions. These crystals are a mixture of difficultly water-soluble hesperidin and readily water-soluble eriodictiol. Recently (1941) a method of producing a solution of citrin from lemon juice suitable for therapeutic use has been developed.

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Eriodictiol is a combination of flavonol with sugar to form a glucoside. Such a combination renders the dye, flavonol, colorless so that in plants the flavonol glucoside is colorless. "Splitting" of the sugar by hydrolysis permits the yellow color to develop.

How is potency expressed?

By actual weight of flavonol glucosides present in a solution determined by iodine titration (Lorenz and Arnold, 1941).

What does Vitamin P do?

It prevents certain types of hemorrhage not due to vitamin C or vitamin K deficiency.

How does it accomplish this effect?

Of it Szent-Gyorgyi says:

"I had a letter from an Austrian colleague who was suffering from a severe hemorrhagic diathesis (vascular type). He wanted to try ascorbic acid in his condition. Possessing at that time no sufficient quantities of crystalline ascorbic acid, I sent him a preparation of paprika that contained much ascorbic acid and the man was cured by it. Later with my friend, St. Ruszynak, we

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tried to produce the same therapeutic effect in similar conditions with pure ascorbic acid but we obtained no response. It was evident that the action of paprika was due to some other substance present in this plant. It would have been a hopeless job to try to find and isolate this substance had we not had our experience with flavons. So we set out to prepare flavons, in the first place eriodictin, that can be easily injected and we found that similar pathological conditions, not previously amenable to therapy, could be cured by it with regularity. The effect had several characteristics of vitamin-action, so, tentatively, I called it "Vitamin P" in honor of Paprika and Permeability, on which later it was found to have an influence. As yet, I have failed to demonstrate its vitamin nature by animal experiments and until such proof is given the vitamin nature of this substance is not beyond doubt."

Kugelmass suggests that, as it is known that in plants glucosides are capable of immobilizing certain other substances until they are needed in metabolism, or in removing the poisons from certain substances, perhaps its protection of the blood vessels is due to this poison-removing

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power. It has been claimed to be effective in reducing blood pressure, in correcting capillary bleeding of allergic individuals, and in the treatment of a skin disease known as psoriasis, but its behavior in these conditions needs further study. It is also not yet certain that the effect of "citrin" preparations is due to a single constituent.

How much do we need?

Kugelmass in his treatment of purpura cases used oral doses of 150 mg. daily of a solution containing 50 mgms. per cc. of citrin.

Where can we get it?

It has been demonstrated to date only in lemon and paprika.

Appendix
Table of Vitamin Contents
of Foodstuffs

VITAMIN CONTENT PER 100 GMS.

Foods	A I.U.	B ₁ I.U.	B ₂ γ	C I.U.
Almonds.....	580 ²⁸	60 ²⁸	600 ¹	0 ¹
Apples.....	75 ¹	8-15 ¹	43 ²⁸	30-400 ¹
Apricots, dried.....	5000 ¹	30 ¹	105 ¹	160 ²⁸
Apricots, fresh.....	4000 ¹	10 ¹	51 ¹	20 ²⁸
Artichokes.....	200 ¹	60 ¹	129 ¹	175 ¹
Asparagus, green.....	700 ¹	65-123 ^{28, 41}	160 ²⁸	348-800 ²⁸
Asparagus, white.....	0-50 ¹	59 ⁴	160 ²⁸	650 ¹
Avocados.....	1000 ¹	34	90 ¹	400 ¹
Bacon.....	25 ¹	33 ²⁸	30 ²¹	0
Banana.....	300 ¹	14-18 ²⁸	50 ²⁸	220 ²⁸
Barley.....	0 ¹	206 ⁴⁴	0 ¹	0
Beans, green.....	1000 ¹	19-24 ^{41, 4}	93 ¹	300 ¹
Beans, dry kidney.....	?	150 ¹	0 ¹	0 ¹
Beans, dry lima.....	100 ¹	170 ⁴	900 ¹	0 ¹
Beans, fresh lima.....	500 ¹	57-114 ^{41, 4}	365 ²⁸	600 ¹
Beans, dry navy.....	0 ¹	128 ¹	1200 ¹	0 ²⁸
Beans, dry soy.....	100 ¹	485 ⁴	900 ¹	0 ¹
Beans, fresh soy.....	200 ¹	175 ¹	300 ¹	800 ¹
Beans, wax.....	0 ¹	24-29 ^{41, 4}	120 ¹	300 ¹
Beef, lean.....	56 ²	25-38 ^{4, 1}	190-375 ^{20, 1}	3.5 ozs.
Beet root.....	tr.	10-17 ^{41, 4}	24-50	100
Blackberries.....	150 ¹	8 ⁴	60 ²⁸	100
Blueberries.....	100 ¹	15 ⁴	90-120 ¹	60
Brain, beef.....	54 ²	56 ²	250 ²⁰	15
Bran, wheat.....	140 ¹	100-360 ²⁸		100
Bread, rye.....	tr.	70 ¹		40

AVE. SERVING VITAMIN CONTENT PER SERVING

Portion	Gms.	A	B ₁	B ₂	C
12-15	15	97	10	100	0
1 small	100	75	8-15	43	30-400
4-6 halves	30	1600	10	33	51
2-3	100	4000	10	51	20
1 large	100	200	60	129	175
4-5, 4" pieces	50	350	32-61	80	174-400
4-5, 4" pieces	50	0-25	29	80	325
1/2	100	1000	34	90	400
3 sl. 4" x 1"	15	4	8	7	0
1	100	300	14-18	50	220
1 tbsp.	14	0	38	0	0
1/2 cup cooked	100	1000	19-24	93	300
1/2 cup cooked	30	?	50	0	0
1/2 cup cooked	30	30	60	300	0
1/2 cup cooked	100	500	57-114	365	600
1/2 cup cooked	30	0	40	400	0
1/2 cup cooked	30	30	160	300	0
1/2 cup cooked	100	200	175	300	800
1/2 cup cooked	100	0	24-29	120	300
3.5 ozs.	100	56	25-38	190-375	100
1/2 cup	100	tr.	10-17	24-50	60
1 cup	100	150	8	15	90-120
3 tbsp.	15	21	15-40		
3.5 ozs.	100	54	56	250	
1 slice	40	tr.	28		

VITAMIN CONTENT PER 100 GMS.					AVE. SERVING VITAMIN CONTENT PER SERVING				
Foods	A I.U.	B ₁ I.U.	B ₂ γ	C I.U.	Portion	Gms.	A	B ₁	B ₂ γ
Cream, 20%.....	680 ¹	10 ⁷			1 oz.	28	200	3	
Cream, 40%.....	1360 ¹				1 tbsp.	15	200		
Cucumber.....	20 ¹	15 ¹	24 ¹	42-100 M	1/4	50	10	8	12
Currents, red.....	15 ¹	15 ¹		300 M	1/4 cup	100		15	21-50
Cocoa.....	25 ⁴								300
Dates, dried.....	150 ¹	25 ¹	45 ¹	0 M	3-4	30	45	7	0
Dates, fresh.....	21 ⁴				6-12	100		21	13
Egg white.....	0 ¹	tr. ⁴	100-220 M	0 M	1	30	0	0	57-90
Egg yolk.....	2800 ¹	118 ⁴	239-385 M	0 M	1	16	448	19	38-62
Eggplant.....	35 ¹	15 ¹	30 ¹	42-100 M	1/4 cup cooked	100	35	15	30
Eggs.....	1000 ¹	50 M	207-248 M	0 M	1	50	500	25	100-125
Endive.....	15000 ¹	33 ⁴	120 ¹	400 ¹	1	50	7500	16	60
Escarole.....	15000 ¹	28 ¹	120 ¹	400 ¹	2 large leaves	50	7500	14	60
Figs, dried.....	60 ¹	22 ¹	75 ¹	0 ¹	2	30	60	22	75
Figs, fresh.....	50 ¹	25 ¹	45 ¹	36 M	3-4	100	50	25	45
Filberts.....	206 M				12	15		31	
Fish, ave. lean.....	tr.	13 M			3-5 ozs.	100		13	
Flour, graham.....	186 M				1 cup	120		213	
Flour, rye.....	56 M		60 M		1 cup	120		67	
Flour, stone ground..	160 M				1 cup	128		205	
Flour, pat. white....	17-33 M ⁴		40 M		1 cup	130		22-30	
Flour, str. white.....	29-50 M ⁴				1 cup	130		38-65	
Flour, white and germ	43 ⁴				1 cup	128		55	
Flour, whole wheat..	160-230 M ⁴ , U. S.		100-200 M		1 cup	128		205-294	

VITAMIN CONTENT PER 100 GMS.

AVE. SERVING VITAMIN CONTENT PER SERVING

Foods	A I.U.	B ₁ I.U.	B ₂ γ	C I.U.	Portion	Gms.	A	B ₁	B ₂	C
Olives, green.....	190 ¹		0 ¹	0 ¹	1	10	19		0	0
Olives, ripe.....	125 ¹	2 ¹	15 ¹	0 ¹	1	5	6	0.1	0.7	0
Onions.....	0 ¹	10 ⁴	123 ¹	200 ¹	1	100	0	10	123	200
Orange juice.....	45-350 ¹	78 ⁴¹	15 ¹	450-1200 ¹	½ cup	100	45-350	78	15	450-1200
Oranges.....	65 ¹	26 ⁴	29 ¹	760-1240 ¹	1	100	65	26	29	760-1240
Pancreas, beef.....			550 ¹⁰		2 ozs.	60			330	
Papaya.....	45-350 ¹	30 ¹	15 ¹	450-1200 ¹	¼	100	45-350	30	15	450-1200
Parsley.....	3000 ¹			2000 ¹	10 sprigs	10	3000			200
Parsnips.....	tr. ¹	40 ¹		258-800 ¹	¼	100	tr.	40		258-800
Pastes (macaroni)...	tr. ¹	16 ¹⁸			¾ cup cooked	30	tr.	4		
Pastes (sago).....	0 ¹	3 ¹⁸			¾ cup cooked	30	0	1		
Pastes (tapioca).....	0 ¹	3 ¹⁸			¾ cup cooked	30	0	1		
Peaches, yellow.....	1000 ¹	10 ¹	60 ¹	140-263 ¹	1	100	1000	10	60	140-263
Peaches, white dry..	3000 ¹	17 ¹		500 ¹	2 halves	30	3000	17		500
Peaches, white.....	5 ¹	8 ⁴		200 ¹	1	100	5	8		200
Peanut butter.....		79								
Peanut germ.....		294 ⁴								
Peanut skin.....		2632 ⁴								
Peanuts.....	0	350 ⁴								
Pears.....	10 ¹	8 ⁴	21 ¹	48-60 ¹	16-17	15	0	53		
Peas, dried.....	520 ¹⁸				1	100	10	8	21	48-60
Peas, dried cow.....		312 ⁴			¾ cup cooked	30				
Peas, green.....	1000 ¹	133 ⁴		300 ¹	¾ cup cooked	30				
Pecans.....	400 ¹	350 ⁴	130-200 ¹	0 ¹	1 cup	100	1000	133	130-200	300
Peppers, red.....	5000 ¹	10 ¹	300 ¹	0 ¹	12 halves	15	60	53	45	0
Peppers, green.....	5000 ¹	10 ¹	138 ¹	4600 ¹	1	100	5000	10	138	4600
			138 ¹	2709 ¹	1	100	5000	10	138	2709

Persimmons.....		820 M	3/4	100			250
Pineapple.....	90 ¹ 30 ⁴	500 M	3/4 cup	100		36	500
Pineapple juice.....	147 ¹¹ 25 ¹¹	140 ¹¹	3/4 cup	100	147	21	140
Plantains.....		14 ¹	1	100			14
Plums.....	16 ⁴	40-116 M	3	100		45	40-116
Pomegranate juice...		120 M	3/4 cup	100			120
Pork, lean.....	300-500 ^{M, 2}		3.5 ozs.	100	300-500	230-390	
Pork, sweet.....	2300 ^M 31 ⁴	160-406 M	1	150	3450	46	102-105
Potato, white.....	30 ¹ 40-62 ⁴	140-300 M	1	150	45	74-93	67-82
Prunes, dried.....	2500 ¹ 60 ⁴	0 M	4-5	50	1250	30	588
Pumpkin.....	2500 ¹ 15 ¹	100 M	3/4 cup cooked	100	2500	15	45
Quince.....		100 M	1	100			100
Radish.....	tr. ¹ 20 ¹	240 M	1	10	tr.	2	24
Radish leaves.....							
Raisins.....	tr. ¹⁰ 33-66 ¹⁰		3/4 cup cooked	100			
Raspberry.....	520 ⁸ 8 ⁴	300 M	3/4 cup	30	157-193	126	
Rhubarb.....	tr. ¹ 8 ⁴	100-200 M	3/4 cup	100	520	8	300
Rice, brown.....	tr. ¹ 159-175 ^M		3/4 cup cooked	30	tr.	8	100-200
Rice, polished.....	tr. ¹ 10 ¹⁰		3/4 cup cooked	30	tr.	48-54	45
Rice polish.....	666-1250 ^M		3/4 cup cooked	30	tr.	3	tr.
Romaine.....	800 ¹		1 oz.	30	198-375		
Rutabaga, white.....	0 ¹ 15 ¹	250 ¹	1 large leaf	10	80	5	25
Rutabaga, yellow....	25 ¹ 25 ⁴	600 M	3/4 cup cooked	100	0	15	600
Rye.....	0 ¹ 131-161 ^{4, 4}	400 ¹	3/4 cup cooked	100	25	25	400
			1 cup	120	0		
Salmon.....	30-750 ¹ tr. ¹		3.5 ozs.	100	30-750	tr.	225
Sardines.....	10 ¹		3 med.	30		3	
Sauerkraut.....	25 ¹ 10 ⁴	0-100 M	3/4 cup	50	15	5	0-50

VITAMIN CONTENT PER 100 GMS.					AVE. SERVING VITAMIN CONTENT PER SERVING				
Foods	A I.U.	B ₁ I.U.	B ₂ γ	C I.U.	Portion	Gms.	A	B ₁	C
Sauerkraut juice.....	35 ⁴			180-206 ³⁸	½ cup	100	35		180-206
Sausage, bologna....	175 ¹				2 slices	30	52		
Sausage, pork.....	115 ¹				2.5 ozs.	75	84		
Shallots.....	300 ¹¹				6	100	300		
Soy beans, dried.....	485 ⁴				½ cup cooked	30	162		
Soy beans, green....	159 ⁴				3.5 ozs.	100	159		
Spinach.....	25000 ¹	35-43 ^{4, 41}	436 ³⁸	1500 ¹	½ cup cooked	100	25000	35-43	1500
Squash, Hubbard...	4000 ¹	16-31 ^{4, 41}	46 ¹	60 ³⁸	½ cup cooked	100	4000	16-31	60
Squash, summer....	1000 ¹	14 ⁴	52 ¹		½ cup cooked	100	1000	14	52
Strawberries.....	740 ⁹	8 ⁴	tr.	720-1300 ³⁸	10	100	740	8	720-1300
Tangerines.....	350 ¹⁰	30 ¹	30 ¹	700 ¹¹	1	100		30	700
Tomato.....	1000 ¹	20-44 ^{4, 41}	38 ³⁸	360-400 ³⁸	1	100	1000	20-44	38
Tomato juice.....	1000 ¹	20-26 ¹	36-174 ¹	250-600 ¹	½ cup	100	1000	20-26	36-174
Tongue, beef.....		100 ¹⁷	220 ³⁸		3.5 ozs.	100		100	220
Trout.....		29 ⁴			3.5 ozs.	100		29	
Turnip, white.....	0 ¹	20 ⁴	42 ²	600 ³⁸	½ cup cooked	100	0	20	600
Turnip, yellow.....	20 ¹	12 ¹	36 ¹	600 ³⁸	½ cup cooked	100	20	12	600
Veal, ave.		40-112 ¹⁷	240-345 ^{38, 3}		3.5 ozs.	100		40-112	240-345
Walnuts.....	120 ⁴⁸	114-140 ^{4, 48}		0 ³⁸	8-15 halves	15	18	17-21	0
Walnuts, English....	100 ¹	150 ⁴		0 ³⁸	8-15 halves	15	15	22	0
Watercress.....	4000 ¹	40 ⁴	270 ¹	1000 ³⁸	10 sprigs	10	400	4	100
Watermelon.....	125 ³⁸	20 ¹	30 ¹	120-300 ³⁸	½ cup	100	125	20	30
Wheat.....	tr. ¹	118-190 ^{4, 48}	105 ¹		½ cup cooked	30	tr.	33-60	120-300
Wheat bran.....		440 ⁴⁸			3 tbsp.	15		66	35

Wheat germ.....	1000 ¹⁸	600-800 ¹⁸
Wines.....		
Yeast, Fl. foil.....	23900	1150
Yeast, bakers dried..	238 ¹⁸	2000-4000 ¹⁸
Yeast, brewers dried..	666 ¹⁸	3770-4230 ¹⁸
Young berry.....	450 ¹⁸	14 ¹

	3-4 ¹⁸	3 thpa. 1 glass	15 100	150	3-4
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1 cake	14	3346	161	210
1 oz.	30		79	
1 oz.	30		333	
1 cup	100	450		14

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